DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Minneapolis District
240 Hennepin Avenue
Minneapolis MN 55401-1999
Telephone: 612-334-4100

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August 11, 1998

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Refer to MIN 98-45

Mogens Pedersen
President of the Skin Care Division
Coloplast Corporation
1940 Commerce Drive
North Mankato, Minnesota 56002

Dear Mr. Pedersen:

On June 22-23, 25 & 30, 1998, the Food and Drug Administration (FDA) conducted an inspection of your drug manufacturing facility in North Mankato, MN. During that inspection our investigator observed and documented serious violations of the current Good Manufacturing Practices (GMPs) for Finished Pharmaceuticals, Title 21, Code of Federal Regulations, Part 211 (21 CFR 211).

The violations observed during our inspection include but are not limited to the following:

1. Failure to establish laboratory controls which include scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, drug product containers, closures, in-process materials, labeling, and drug products conform to appropriate standards of identity, strength, quality, and purity (21 CFR 211.160). For example,

(A) Your microbiology lab sterilizer has not been validated, or otherwise studied, checked, or maintained to determine proper functioning, or to indicate the lethality to which maximum and minimum loads are subjected.
(B) No growth promotion testing has been performed with microbiology media, or other positive controls used with testing, to show the media is capable of growing organisms.
(C) The water system used to manufacture a variety of drug products has not been validated.

2. Failure to withhold from use each lot of components until the lot has been sampled, tested, or examined, as appropriate, and released for use by the quality control unit (21 CFR 211.84). For example,

(A) The water system used to manufacture a variety of drug products has not been validated.

3. Failure to thoroughly investigate the failure of a batch or any of its components to meet specifications (21 CFR 211.192). For example:

(A) There is no documentation of follow-up to out-of-specification water microbiological results.
(B) Not all batch failures are investigated.

4. Failure to have a written testing program designed to assess the stability characteristics of drug products (21 CFR 211.166). For example:

(A) There is no written procedure to cover accelerated stability testing or testing of an adequate number of batches.

5. Failure to determine the expiration date of a drug product using appropriate stability testing (21 CFR 211.137). For example:

(A) There is no stability data to support the Sea-Clens expiration date of two years.

The violations of the Act described above are not meant to be an all-inclusive list of deficiencies at your firm. It is your responsibility to ensure that all drug products manufactured and distributed by your firm are in compliance with this statute. Federal agencies are advised of the issuance of all Warning Letters about drugs and devices so they may take this information into account when considering the award of contracts.

We request you take prompt action to correct these violations. Failure to promptly correct them may result in regulatory action without further notice. This action may include seizure and/or injunction.

Please respond to this office in writing within 15 working days of receiving this letter. Your response should describe the specific actions you will take, or have taken, to correct the noted violations. Your response should also include an explanation of each step being taken to prevent recurrence of similar violations. If corrective action cannot be completed within 15 working days, please state the reason for the delay and time within which corrections will be completed.

In addition, we have become aware that you may be marketing unapproved new drugs. For example:

* Antimicrobial and antifungal drug products are subject to the regulations of 21 CFR 333: Topical Antimicrobial Drug Products for Over-the-Counter Human Use. Chloroxylenol is not an approved ingredient of antimicrobial or antifungal drug products.
* Products making psoriasis claims are subject to the regulations of 21 CFR 358 Subpart H: Drug products for the Control of Dandruff, Seborrheic Dermatitis, and Psoriasis. Products regulated by this subpart may only contain the active ingredient coal tar, 0.5 to 5 percent, or salicylic acid, 1.8 to 3 percent. No other active ingredients are approved for the treatment of psoriasis.
* Anorectal products are subject to the requirements of 21 CFR 346: Anorectal Drug Products for Over-the-Counter Human Use. Zinc oxide may not be used as a sole protectant active ingredient but may be used in combination with up to three other approved active ingredients. Benzethonium chloride is not an approved active ingredient for products of this type.

For your information, the safety and effectiveness of diaper rash ointments [Over-the-Counter (OTC) drug products] are being evaluated by the FDA under OTC Drug Review. Proposed regulations affecting these drugs have been published in the Federal Register as follows: 55 FR 25204, June 20, 1990, Tentative Final Monograph for Skin Protectant Drug Products for Over-The-Counter Human Use. The proposed regulations may be used as guidelines in formulating and labeling OTC drug products. You may check your local library or contact the Food and Drug Administration, Division of Communications Management (HFD-210), Center for Drug Evaluation and Research, 5600 Fishers Lane, Rockville, Maryland 20857 (1-301-827-4573) for copies of this Federal Register notice. Pending issuance of final regulations, the Agency does not object to the marketing of OTC drugs that meet both the formulation and labeling requirements described in these proposals. Such marketing, however, is subject to the risk that it may be necessary to reformulate and/or re-label these products, or seek FDA approval through the "new drug" provisions of the Act once a final rule is in effect.

We acknowledge receipt of your firm's July 14, 1998, response, signed by Don Gerrish, Director of Quality Assurance, to the items cited on the form FDA-483 issued to Douglas J. Rohlk on June 30, 1998. The response is under review.

Your reply to the noted violations should be sent to Compliance Officer Carrie A. Hoffman at the address indicated on the letterhead.

Sincerely,

James A. Rahto
District Director
Minneapolis District

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